

II. REMARKS

Upon entry of the amendment, claims 1 to 18 will be pending.

Pursuant to the Restriction Requirement, claims 19 to 26 are cancelled herein without disclaimer, and without prejudice to Applicants' pursuing prosecution of subject matter encompassed within one or more of the claims in an application claiming the benefit of priority of the subject application.

A. Regarding the Restriction Requirement

It is alleged in the Office Action that the claims are directed to four distinct inventions, which were set out as Groups I to IV, as follows:

Group I: claims 1 and 4 to 16, directed to methods of inhibition proliferation of tumor cells by antisense inhibition of a type II hexokinase mRNA;

Group II: claims 1 to 3 and 6 to 16, directed to methods of inhibition proliferation of tumor cells by antisense inhibition of type I hexokinase mRNA;

Group III: claims 17 and 18, directed to a pharmaceutical preparation comprising antisense targeted to a hexokinase mRNA; and

Group IV: claims 19 to 26, directed to a nucleic acid vector, which can include a hexokinase complementary sequence and a recombinant nucleic acid comprising a sequence complementary to a hexokinase.

It is further stated that, with respect to Group IV, the invention includes two distinct species, set forth as 1) the complement to SEQ ID NO:1 (type II hexokinase); and 2) the complement to SEQ ID NO:2 (type I hexokinase). As such, it is requested that, if Group IV is elected, that a species of complementary nucleic acid further be elected.

Although the restriction requirement is traversed, in part, for the reasons set forth below, Applicants nevertheless provisionally elect the claims of **Group II, claims 1 to 3 and 6 to 16**, in order to be responsive to the Restriction Requirement. Although it is indicated in the Office Action that Group II is directed to methods of using an antisense targeted to **type I** hexokinase, Applicants point out that the claims of Group II, in fact, are directed to use of an antisense targeted to **type II** hexokinase (see claim 3; see also, claim 2, wherein SEQ ID NO:1 encodes rat mutant type II hexokinase; see, also, legend to Figure 6 at page 3, and Figure 6).

As such, Applicants elect with traverse Group II, claims 1 to 3 and 6 to 16, directed to methods of inhibition proliferation of tumor cells by antisense inhibition of **type II** hexokinase mRNA. The restriction requirement is traversed with respect to the division of the claims of Group I from those Group II, and further with respect to the division of the claims of Group III from those of Group II.

1. Traversal with respect to Groups I and II

With respect to the traversal of the division of the claims of Group I from those of Group II, it is stated in the Office Action that "Inventions I and II are unrelated." (page 3, first full paragraph). Applicants submit, however, that the Groups I and II are related in that claim 1 is generic (i.e., directed to use of an antisense to inhibit a "hexokinase") with respect to the subject matter of claims 3 and 4, wherein the hexokinase comprises a subgenus (i.e., "type II" hexokinase and "type I" hexokinase, respectively), and further with respect to claims 2 and 5, wherein the hexokinase is a species (i.e., SEQ ID NO:1 and SEQ ID NO:2, respectively). In this respect, it is noted that Office Action acknowledges the "Claims 1 and 6 to 16 are generic to Groups I and II" and further requires that, if Group IV is elected, a species set forth as the complement of SEQ ID NO:1 (type II hexokinase) or the complement of SEQ ID NO:2 (type I hexokinase) be elected.

Further with respect to the relatedness of SEQ ID NO:1 and SEQ ID NO:2 and, therefore, their complements, a BLASTN comparison of the sequences is attached as Exhibit A. As is evident from the two way BLAST, SEQ ID NOS:1 and 2 share substantial sequence identity, including, for example, 74% identity in the 1144 nucleotide sequence encoding amino acid residues 527 to 907; 77% identity in the 638 nucleotide sequence encoding amino acid residues 110 to 322; and 81% identity in the 113 nucleotides encoding amino acid residues 431 to 468. For the Examiner's convenience, a comparison of the encoded type I and type II hexokinase sequences is attached as Exhibit B, with the above-mentioned amino acid sequences highlighted. In view of the substantial sequence identity shared among SEQ ID NO:1 and SEQ ID NO:2, it is submitted that an antisense polynucleotide useful for inhibiting expression, for example, of a type II hexokinase would similarly be useful for inhibiting expression of a type I hexokinase. Further in this respect, it is disclosed in the specification that it is "highly likely" that the antisense polynucleotide used in the exemplified methods, which was generated from the type II hexokinase sequence, also targeted the type I hexokinase mRNA (see paragraph bridging pages 40 to 41 of the specification).

In summary, it is clear from the language of the claims that claim 1 is generic with respect to the subgenera type I and type II hexokinases, and from the BLASTN comparison (Exhibit A) that the hexokinases set forth as SEQ ID NO:1 and SEQ ID NO:2 are related species of hexokinase, and is acknowledged in the Office Action that the complements of SEQ ID NO:1 and SEQ ID NO:2 are species. Accordingly, it is submitted that the division of claims 1 to 16 into two separate Groups based on the species of hexokinase recited in the claims is improper, and respectfully requested that the division of the claims of Group I and Group II be withdrawn and claims 1 to 16 be examined together. Alternatively, it is respectfully requested that a species requirement be made, in which case, Applicants would elect the species set forth as the complement of SEQ ID NO:1 (antisense specific for type II hexokinase; claims 1 to 3 and 6 to 16), and would request that, upon a determination being made that the subject matter of

claims 1 to 3 and 6 to 16 is allowable, that the species set forth in claims 4 and 5 further be examined.

2. Traversal with respect to Groups II and III

It is stated in the Office Action that the claims of "Inventions (I and II) and III are related as product and process of use", and suggested, for example, that "the methods of groups I and II could be performed via the expression of hexokinase antisense transcripts [from] a vector." (page 4, first paragraph). Applicants point out, however, that a search of the claims of provisionally elected Group II would, of necessity, require a search of hexokinase antisense sequence sequences because such sequences are required for practicing the claimed methods. Further, the methods of Groups I and II can be practiced *in vivo* (see, e.g., claim 13) and, therefore, a search of such claims would, of necessity, require a search of pharmaceutical preparations that contain such hexokinase antisense molecules (i.e., the subject matter of claims 17 and 18). As such, any search of the claims of Group II (and Group I, if rejoined) would be coextensive with and reveal art relevant to the subject matter of claims 17 and 18. Accordingly, it would not be an undue burden for the Examiner to rejoin claims 17 and 18 with provisionally elected claims 1 to 3 and 6 to 16 and, therefore, respectfully requested that the claims of Groups II and III be rejoined and examined together.

In summary, the claims of Group II, claims 1 to 3 and 6 to 16, are provisionally elected for examination. However, for the reasons set forth above, it is respectfully requested that the Examiner reconsider the Restriction Requirement and examine the claims of Groups I, II and III together. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

In re Application of
Pedersen and Mathupala
Application No.: 09/808,743
Filed: March 14, 2001
Page 9

PATENT
Attorney Docket No.: JHU1720-1

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: May 12, 2003



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San Diego, CA 92121-2133

Enclosures: Exhibits A and B

EXHIBIT A



Blast 2 Sequences results

PubMed

Entrez

BLAST

OMIM

Taxonomy

Structure

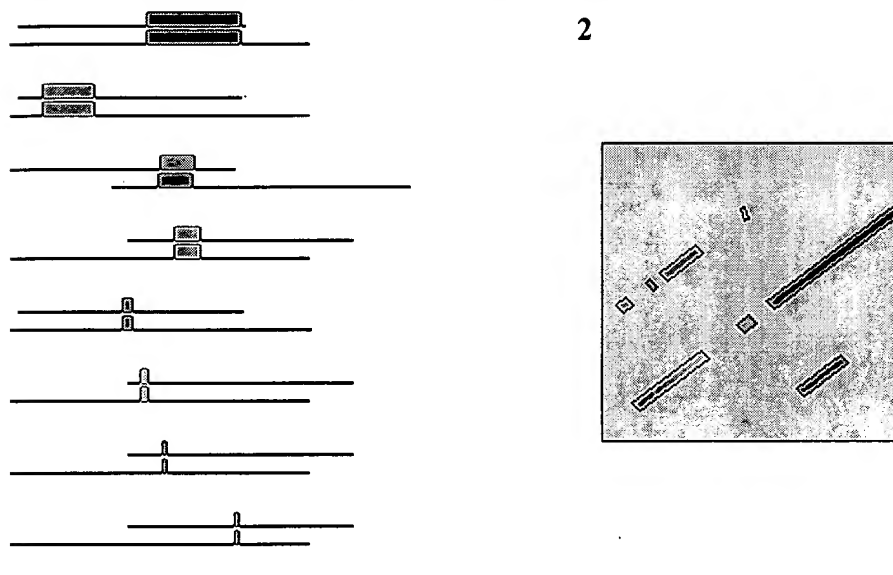
BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.5 [Nov-16-2002]

Match: Mismatch: gap open: gap extension:
 x_dropoff: expect: wordsize: Filter ☒

Sequence 1 gi 2689657

Length 2754 (1 .. 2754)

Sequence 2 gi 6981021 Rattus norvegicus Hexokinase 1 (Hk1), mRNA Length 3653 (1 .. 3653)



NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

NOTE: If protein translation is reversed, please repeat the search with reverse strand of the query sequence

Score = 492 bits (256), Expect = e-135

Identities = 848/1144 (74%)

Strand = Plus / Plus

```

Query:      1579 gacttcttggccttggatcttggaggaacaaacttcggggtcctgctggtgctgtgcgt 1638
             ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct:      1670 gacttcctggccttggatcttggaggaacgaatttcggggttctgctggttaaagatccgc 1729
hexokinase 1 527 D F L A L D L G G T N F R V L L V K I R
  
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Query:      1639 aatggcaagcggaggggctggagatgcataacaagatctactccatcccacaggaggtt 1698
             | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Sbjct:      1730 agtgggaaaaagagaacagtggaaatgcacaacaagatctactccattcccctggaaatc 1789
hexokinase 1 547 S G K K R T V E M H N K I Y S I P L E I
  
```

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Query:      2239  ggcatgtacttgggagagattgtgcgcaacattctcatcgatttcacgaagcggggggctg 2298
            ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||
Sbjct:      2330  gggatgtacctgggtgagatcgtcgtaacatcctgattgacttcaccaagaaaggcttc 2389
hexokinase 1 747  G M Y L G E I V R N I L I D F T K K G F

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Query: 2299 ctcttccgaggccgcacatctcagagcgccctcaagacaaggggaatctctgaaactaagttc 2358
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Sbjct: 2390 ctcttccggggacagatctccgaaccactcaagacccgaggcatctttgagaccaagttt 2449
hexokinase 1 767 L F R G Q I S E P L K T R G I F E T K F

Query: 2359 ctgtctcagatagagagcgactgcctagccctgctacagggttcgtgccatcctgcgccac 2418
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Query: 2419 ctagggctggagagcacgtgcgatgacagcatcatcgtagaggaggtgtgcactgtgggtt 2478
|| || ||||| ||||| ||||| ||||| ||||| ||||| |||||
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hexokinase 1 807 L G L N S T C D D S I L V K T V C G V V

Query: 2479 gcccggcgcgctgcacagctctgtggcgaggcatggccgccgtagtggacaagataaga 2538
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Sbjct: 2570 tccaagagggcggtcagctgtgtggtgccggcatggccgccgtggtggaaaagatcaga 2629
hexokinase 1 827 S K R A A Q L C G A G M A A V V E K I R

Query: 2539 gagaaccgtgggctgggacaaccccaaagtgcagtgggcggtggacgggactctgtataag 2598
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Query: 2599 cttcatcctcactttgccaaaggtcatgcatgagacgggtgagagatctggctccgaaatgt 2658
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Query: 2659 gacgtgtccttccctggaatccgaggacggcagtggaagggagcagctctcatcactgcc 2718
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hexokinase 1 887 T V S F L L S E D G S G K G A A L I T A

Query: 2719 gtgg 2722
||||
Sbjct: 2810 gtgg 2813
hexokinase 1 907 V

Score = 385 bits (200), Expect = e-103
Identities = 492/638 (77%)
Strand = Plus / Plus

Query: 329 agatctacgccatccttgaggacatcatgcggggcagtggaaccagctgtttgaccaca 388
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Sbjct: 420 agatctacgacacccagagaaacatcgatggcagtggaaccagcttttcgatcatg 479
hexokinase 1 110 E I Y D T P E N I V H G S G T Q L F D H

Query: 389 tcgccgaatgcctggccaacttcatggacaagctacaaatcaaagagaagaagctccctc 448
||||| ||| ||||| ||||| ||||| ||| ||||| ||| ||||| |||
Sbjct: 480 tcgctgactgcctgggagacttcatggagaaaaagaagatcaaggacaagaagttaccgcg 539
hexokinase 1 130 V A D C L G D F M E K K K I K D K K L P

Query: 449 tgggtttcaccttctcgttcccctgccaccagacaaaactggatgagagtttttgggtct 508
||||| ||||| ||| ||| ||||| ||||| ||| ||| ||| ||||| ||| ||| |||
Sbjct: 540 tgggattcacattttccttcccctgccgacaatccaagatagatgaggctgtactgatca 599
hexokinase 1 150 V G F T F S F P C R Q S K I D E A V L I

Query: 509 cgtggactaaggggttcaagtccagtggcgtggaaggcagagatgtggtggacctgatcc 568
||||||| ||| ||||| ||||| ||||| ||||| ||||| ||| ||| |||
Sbjct: 600 cgtggacaaagcggttcaaagccagtggcgtggaaggagcggatgtggtcaagttgctga 659
hexokinase 1 170 T W T K R F K A S G V E G A D V V K L L

Query: 569 ggaaggttatccagcgcagaggggactttgacattgacattgtggccgtggtgaatgaca 628
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hexokinase 1 190 N K A I K K R G D Y D A N I V A V V N D

Query: 629 cagttgggaccatgatgacttgtggctatgatgatcagaactgagagattggtctcattg 688
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Sbjct: 720 cagtagggaccatgatgacctgcggttatgatgaccaacagtgtgaagtgcgcctgatca 779
hexokinase 1 210 T V G T M M T C G Y D D Q Q C E V G L I

Query: 689 tgggcactggcagcaacgcctgctacatggaggaaatgcgatcatattgacatgggtggagg 748
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hexokinase 1 230 I G T G T N A C Y M E E L R H I D L V E

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hexokinase 1 250 G D E G R M C I N T E W G A F G D D G S

Query: 809 tcaatgacatccgaaccgagtttgaccgagagatcgacatgggctcgctgaaccctggga 868
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Sbjct: 900 tggaagacatccgaaccgagtttgacagagagtttagaccgtggatctctcaaccctggga 959
hexokinase 1 270 L E D I R T E F D R E L D R G S L N P G

Query: 869 agcagctgtttgagaagatgattagcgggatgtacatgggggagctgggtcaggctcatcc 928
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hexokinase 1 290 K Q L F E K M V S G M Y M G E L V R L I

Query: 929 tgggtgaagatggccaaggcagagctgttgttccaaggg 966
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Score = 183 bits (95), Expect = 1e-42

Strand = Plus / Plus

Strand = Plus / Plus

5/6/2003

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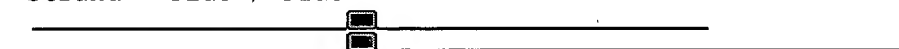
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Query: 766 tgcataacatggagtgaggcctttggggacgacgggtacactcaatgacatccgaacc 825
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hexokinase 1 704 C I N M E W G A F G D N G C L D D I R T

Query: 826 gagtttgaccgagagatcgacatgggctcgctgaaccctgggaagcagctgtttgagaag 885
|| ||||| || | | ||| || ||||| || ||||| ||
Sbjct: 2261 gactttgacaaagtgggtggacgaatattctctaaactctgggaacaaagggttgagaaa 2320
hexokinase 1 724 D F D K V V D E Y S L N S G K Q R F E K

Query: 886 atgattagcgggatgtacatgggggag 912
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Sbjct: 2321 atgatcagtgggatgtacctgggtgag 2347
hexokinase 1 744 M I S G M Y L G E

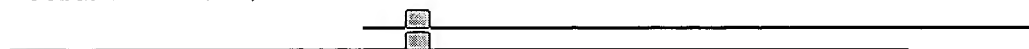
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Identities = 92/113 (81%)
Strand = Plus / Plus



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|||| | ||||| |||| || ||||| ||||| ||| ||| ||||| ||||
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hexokinase 1 431 L R R L V P D S D V R F L L S E S G T G

Query: 1352 agggggctgctatggtgacggcggtggcttacgctctggctgaccaacaccgg 1404
|||||| | ||||| |||| || ||||| ||||| || |||||
Sbjct: 1443 agggggccgcatggtgacggcagtagcctaccgctggctgagcagcaccgg 1495
hexokinase 1 451 K G A A M V T A V A Y R L A E Q H R

Score = 71.8 bits (37), Expect = 6e-09
Identities = 75/94 (79%)
Strand = Plus / Plus



Query: 179 ctgtgaaaatggtgcctacctttgtgaggtcaactccggatgggacagaacatggggagt 238
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Sbjct: 1614 ctgtcaaaaatgctgccttcttttgtccggagcatcccgatgggactgaacacggtgact 1673
hexokinase 1 508 T V K M L P S F V R S I P D G T E H G D

Query: 239 tcctggctctggatcttggaggaaccaacttcg 272
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hexokinase 1 528 F L A L D L G G T N F R

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Strand = Plus / Plus

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Sbjct: 1880 cctctgggtttcaccttctcatttccctgccatcagacgaacctgga 1926
hexokinase 1 597 P L G F T F S F P C H Q T N L D

Score = 46.8 bits (24), Expect = 0.19
Identities = 32/36 (88%)
Strand = Plus / Plus

Query: 1323 cttcctccgctctgaggatggcagcggcaagggggc 1358
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Sbjct: 2758 cttcctcctgtctgaagacggcagcggcaagggggc 2793
hexokinase 1 890 F L L S E D G S G K G A

CPU time: 0.15 user secs. 0.04 sys. secs 0.19 total secs.

Lambda	K	H
1.33	0.621	1.12

Gapped

Lambda	K	H
1.33	0.621	1.12

Matrix: blastn matrix:1 -2
Gap Penalties: Existence: 5, Extension: 2
Number of Hits to DB: 22
Number of Sequences: 0
Number of extensions: 22
Number of successful extensions: 17
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
Number of HSP's successfully gapped in prelim test: 0
Number of HSP's that attempted gapping in prelim test: 0
Number of HSP's gapped (non-prelim): 10
length of query: 2754
length of database: 8,529,560,197
effective HSP length: 26
effective length of query: 2728
effective length of database: 8,529,560,171
effective search space: 23268640146488
effective search space used: 23268640146488
T: 0
A: 0
X1: 6 (11.5 bits)

X2: 26 (50.0 bits)
S1: 12 (23.8 bits)
S2: 22 (43.0 bits)

EXHIBIT B



Blast 2 Sequences results

PubMed

Entrez

BLAST

OMIM

Taxonomy

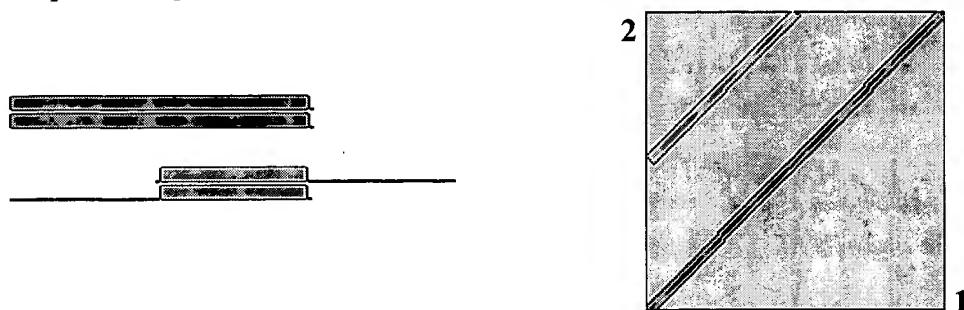
Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.5 [Nov-16-2002]

Matrix **BLOSUM62** gap open: **11** gap extension: **1**
 x_dropoff: **50** expect: **10.000** wordsize: **3** Filter ☒ **Align**

Sequence 1 gi 6981022 hexokinase 1 [Rattus norvegicus] **Length** 918 (1 .. 918)

Sequence 2 gi 2689658 mutant type II hexokinase [Rattus norvegicus] **Length** 917 (1 .. 917)



NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database

Score = 1352 bits (3500), Expect = 0.0

Identities = 652/912 (71%), Positives = 781/912 (85%)

```

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Sbjct: 1  MIASHMIACLFTELNQNVQVQKVDQFLYHMRLSDETLLEISRFRKEMEKGLGATTHPTAA 60

Query: 61 VKMLPTFVRSIPDGSEKGFIALDLGSSFRILRVQVNHEKNQNVSMESSEIYDTPENIVH 120
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Sbjct: 61 VKMLPTFVRSTPDGTEHGEFLALDLGGTNFRVLRVRVTDNGLQRVEMENQIYAILEDIMR 120

Query: 121 GSGTQLFDHVADCLGDFMEXXXXXXXXXXLPVGFTFSFPCRQSKIDEAVLITWTKRFKASGV 180
        GSGTQLFDH+A+CL +FM+ LP+GFTFSFPC Q+K+DE+ L++WTK FK+SGV
Sbjct: 121 GSGTQLFDHIAECLANFMDKLQIKEKKLPLGFTFSFPCHTKLDESFLVSWTKGFKSSGV 180

Query: 181 EGADVVKLLNKAIKKRGDYDANIVAVVNDTVGTMTCGYDDQQCEVGLIIGTGTNACYME 240
        EG DVV L+ K I++RGD+D +IVAVVNDTVGTMTCGYDDQ CE+GLI+GTG+NACYME
Sbjct: 181 EGRDVVDLIRKVIQRRGDFDIDIVAVVNDTVGTMTCGYDDQNCIEIGLIVGTGSNACYME 240

Query: 241 ELRHIDLVEGDEGRMCINTEWGAFGDDGSLEDIRTEFDRELDRGSLNPGKQLFEKMOVSGM 300
        E+RHID+VEGDEGRMCIN EWGAFGDDG+L DIRTEFDRE+D GSLNPGKQLFEKM+SGM
Sbjct: 241 EMRHIDMVEGDEGRMCINMEWGAFGDDGTLNDRTEFDREIDMGSLNPGKQLFEKMISGM 300

Query: 301 YMGEVLRLILVKMAKEGLLFEGRITPELLTRGKFNTSDVSAIEKDKEGIQNAKEILTRLG 360
        YMGEVLRLILVKMAK LLF+G+++PELLT G F T DVS IE+DK+GI+ A +IL RLG
Sbjct: 301 YMGEVLRLILVKMAKAEELLFQGLSPPELLTTGSFETKDVSDIEEDKDGIEKAYQILMRLG 360

Query: 361 VEPSDVDCVSVQHICTIVSFRSANLVAATLGAILNRLRDNKGTPLRLTTVGVDGSLYKMH 420
        + P DCV+ IC IVS RSA+L AATL A+L R+++NKG RLR+T+GVDGS+YK H
  
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Sbjct: 361 LNPLQEDCVATHRICQIVSTRSASLCAATLA AVLWRIKENKGEERLRSTIGVDGSVYKKH 420

Query: 421 PQYSRRFHKTLRRLVPSDVRFLLESSEGTGKGAAMVTAVAYRLAEQHRQIEETLAHFRLS 480
P +++R HK +RRLVPD DVRFL SE G+GKGAAMVTAVAYRLA+QHR ++TL +LS

Sbjct: 421 PHFAKRLHKAVRRLVPDCDVRFLRSEDGSGKGAAMVTAVAYRLADQHRARQKTLESCLKS 480

Query: 481 KQTLMEVKKRLRTEMEMGLRKETNSKATVKMLPSFVRSIPDGTEHGDFLALDLGGTNFRV 540
+ L+EVK+R++ EME GL KET++ A VKMLP++V + PDGTE GDFLALDLGGTNFRV

Sbjct: 481 HEQLLEVKKRMKVEMEQLSKETHAVAPVKMLPTYVCATPDGTEKGDFLALDLGGTNFRV 540

Query: 541 LLVKIRSGKKRTVEMHNKIYSIPLEIMQGTGDELFDHIVSCISDFLDYMGIKGPRMPLGF 600
LLV++R+GK+R VEMHNKIYSIP E+M GTG+ELFDHIV CI+DFL+YMG+KG +PLGF

Sbjct: 541 LLVRVRNGKRRGVEMHNKIYSIPQEVMHGTGEELFDHIVQCIADFLEYMGMKGVSLPLGF 600

Query: 601 TFSFPCHQTNLDGILISWTKGFKATDCEGHDVASLLRDAVKRREEFDLDVVAVVNDTVG 660
TFSFPC Q +LD IL+ WTKGFKA+ CEG DV +LL++A+ RREEFDLDVVAVVNDTVG

Sbjct: 601 TFSFPCQQNSLDQSILLKWTGFKASGCEGEDVVTLLKEAIHRREEFDLDVVAVVNDTVG 660

Query: 661 TMMTCAYEPTCEIGLIVGTGTNACYMEEMKNVEMVEGNQGMCMINMEWGAFGDNGCLDD 720
TMMTC YE+P CE+GLIVGTG+NACYMEEM+NVE+V+G +G+MC+NMEWGAFGDNGCLDD

Sbjct: 661 TMMTCGYEDPHCEVGLIVGTGSNACYMEEMRNVELVDGEEGRMCVNMEWGAFGDNGCLDD 720

Query: 721 IRTDFDKVVDEYSLNSGKQRFKEMISGMYLGEIVRNILIDFTKKGFLFRGQISEPLKTRG 780
+RT FD VDE SLN GKQRFKEMISGMYLGEIVRNILIDFTK+G LFRG+ISE LKTRG

Sbjct: 721 LRTVFDVADELNPGKQRFKEMISGMYLGEIVRNILIDFTKRGLLFRGRISERLKTRG 780

Query: 781 IFETKFLSQIESDRLALLQVRAILQQGLNSTCDDSIIVKTVCGVVSRAAQLCGAGMAA 840
I ETKFLSQIESD LALLQVRAIL+ LGL STCDDSI+VK VC VV++RAAQLCGAGMAA

Sbjct: 781 ISETKFLSQIESDCLALLQVRAILRHLGLESTCDDSIIVKEVCTVVARAAQLCGAGMAA 840

Query: 841 VVEKIRENRGLDHLNVTVGVDGTLYKLHPHFSRIMHQTVKELSPKCTVSFLLSEDGSGKG 900
VV+KIRENRGLD+ VTVGVDGTLYKLHPHF+++MH+TV++L+PKC VSFL SEDGSGKG

Sbjct: 841 VVDKIRENRGLDNPKVTVGVDGTLYKLHPHFAKVMHETVRDLAPKCDVSFLESEDGSGKG 900

Query: 901 AALITAVGVRLR 912
AALITAV R+R

Sbjct: 901 AALITAVACRIR 912

Score = 509 bits (1311), Expect = e-142

Identities = 239/449 (53%), Positives = 334/449 (74%)

Query: 17 DQVKKIDKYLYAMRLSDEILIDILTRFKKEMKNGLSRDYNPTASVKMLPTFVRSIPDGSE 76
DQ + K L +++LS E L+++ R K EM+ GLS++ + A VKMLPT+V + PDG+E

Sbjct: 465 DQHRARQKTLESCLKLSHEQLLEVKKRMKVEMEQLSKETHAVAPVKMLPTYVCATPDGTE 524

Query: 77 KGDFIALDLGGSSFRILRVQVNHEKNQNVSMESSEIYDTPENIVHSGTQLFDHVADCLGD 136
KGDF+ALDLGG++FR+L V+V + K + V M ++IY P+ ++HG+G +LFDH+ C+ D

Sbjct: 525 KGDFLALDLGGTNFRVLLVRVRNGKRRGVEMHNKIYSIPQEVMHGTGEELFDHIVQCIAD 584

Query: 137 FMEXXXXXXXXXLPVGFTFSFPCRSKIDEAVLITWTKRFKASGVEGADVVKLLNKAIKKR 196
F+E LP+GFTFSFPC+Q+ +D+++L+ WTK FKASG EG DVV LL +AI +R

Sbjct: 585 FLEYMGMKGVSLPLGFTFSFPCQQNSLDQSILLKWTGFKASGCEGEDVVTLLKEAIHRR 644

Query: 197 GDYDANIVAVVNDTVGTMTCGYDDQCEVGLIIGTGTNACYMEELRHIDLVEGDEGRMC 256
++D ++VAVVNDTVGTMTCGY+D CEVGLI+GTG+NACYMEE+R+++LV+G+EGRMC

Sbjct: 645 EEFDLDVVAVVNDTVGTMTCGYEDPHCEVGLIVGTGSNACYMEEMRNVELVDGEEGRMC 704

Query: 257 INTEWGAFGDDGSLEDIRTEFDRELDRLNPGKQLFEKVMVSGMYMGELVRLILVKMAKE 316

+N EWGAFGD+G L+D+RT FD +D SLNPGKQ FEKM+SGMY+GE+VR IL+ K
Sbjct: 705 VNMEWGAFGDNGCLDDLRTVFDVAVDELSLNPGKQRFKISMISGMYLGEIVRNILIDFTKR 764

Query: 317 GLLFEGRITPELLTRGKFNTSDVSAIEKDKEGIQNAKEILTRLGVPSDVDCVSVQHICT 376
GLLF GRI+ L TRG T +S IE D + + IL LG+E + D + V+ +CT
Sbjct: 765 GLLFRGRISERLKTGRGISETKFLSQIESDCLALLQVRAILRHLGLESTCDDSIIVKEVCT 824

Query: 377 IVSFRSANLVAATLGAILNRLRDNKGTPRLRTTVGVDGSLYKMHQPYSRRFHKTLLRRLVP 436
+V+ R+A L A + A++++R+N+G + TVGVDG+LYK+HP +++ H+T+R L P
Sbjct: 825 VVARRAAQLCGAGMAAVVDKIRENRGLDNPKVTVGVDGTLYKLHPHFAKVMHETVRDLAP 884

Query: 437 DSDVRFLLSSESGTGKGAAMVTAVAYRLAE 465
DV FL SE G+GKGAA++TAVA R+ E
Sbjct: 885 KCDVSFLESEDGSGKGAALITAVACRIRE 913

CPU time: 0.21 user secs. 0.05 sys. secs 0.26 total secs.

Lambda	K	H
0.321	0.138	0.401

Gapped

Lambda	K	H
0.267	0.0410	0.140

Matrix: BLOSUM62

Gap Penalties: Existence: 11, Extension: 1

Number of Hits to DB: 9329

Number of Sequences: 0

Number of extensions: 580

Number of successful extensions: 3

Number of sequences better than 10.0: 1

Number of HSP's better than 10.0 without gapping: 1

Number of HSP's successfully gapped in prelim test: 0

Number of HSP's that attempted gapping in prelim test: 0

Number of HSP's gapped (non-prelim): 2

length of query: 918

length of database: 459,195,910

effective HSP length: 137

effective length of query: 781

effective length of database: 459,195,773

effective search space: 358631898713

effective search space used: 358631898713

T: 9

A: 40

X1: 16 (7.4 bits)

X2: 129 (49.7 bits)

X3: 129 (49.7 bits)

S1: 41 (21.8 bits)

S2: 80 (35.4 bits)